CENTER FOR DRUG EVALUATION AND RESEARCH

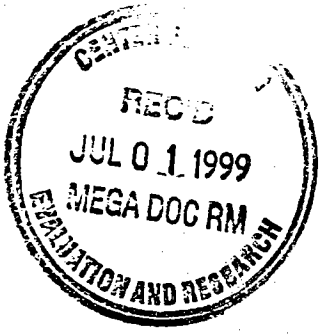
APPLICATION NUMBER: 020968

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

ORIGINAL

Advanced Care Products
Personal Products Company
691 Highway 1, P.O. Box 6024
North Brunswick, New Jersey 08902-0724

NEW CORRESP
NC



June 30, 1999

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

GENERAL CORRESPONDENCE
Pending NDA 20-968
Miconazole Nitrate Vaginal [redacted] and External Cream

Dear Dr. Goldberger:

Reference is made to pending NDA 20-968 for the prescription use of a 1200 mg miconazole nitrate vaginal [redacted] and 2% external cream for treating vaginal candidiasis. Reference is also made to our teleconference today, June 30, 1999 in which FDA and Advanced Care Products ACP) agreed to the following changes for the labeling of the subject NDA. The agreements are as follows:

1. On the Package Carton, Physician Package Insert, Patient Package Insert, and Blister, the established name will be *at least* half the size of the trade name, using the letter "L" as a reference.
2. As agreed to in our submission of June 29, 1999, in the **"Microbiology"** section of the physician package insert, third paragraph, we will change the phrase [redacted]
3. In the Physician Package Insert, **"Warnings"** section, change [redacted]
4. In the Patient Package Insert, statement #1 under the heading **"What is the MONISTAT® DUAL-PAK™?"** we will remove the hyphen [redacted]
5. In the Patient Package Insert under the heading **"What warnings should I know about when using the MONISTAT® DUAL-PAK™?"** we will revise the statement [redacted]

We commit that the Final Printed Labeling (FPL) will reflect the above-specified changes. If you have any questions, please contact me directly at 732-524-1675.

Sincerely,
ADVANCED CARE PRODUCTS

Diane Herron

Diane Herron
Director, Regulatory Affairs

cc: Dr. Christina Chi, Project Manager, DSPIDP (HFD-590)

ORIGINAL NEW DRUG APPLICATION
NDA 20-968
MICONAZOLE NITRATE (1200 mg) VAGINAL OVULE
ITEM 13: PATENT INFORMATION

As per 21 CFR § 314.53, we hereby submit the following patent information.

(i) Patent Number: 5,514,698

Date of Patent Expiration: March 21, 2014

(ii) Type of Patent: Drug Product

(iii) Patent Owner: Advanced Care Products, Ortho Pharmaceutical Corporation*, Raritan, NJ

(iv) Patent Owner does have a place of business in the United States.

The undersigned declares that Patent No. 5,514,698 covers the formulation and composition of the miconazole nitrate 2% external vulvar cream. This product is used in conjunction with miconazole nitrate 1200 mg vaginal ovule. These two products together are the subject of this application for which approval is being sought.

* Ortho Pharmaceutical Corporation is an affiliate of Johnson & Johnson. Advanced Care Products (ACP) was a division of Ortho Pharmaceutical Corporation. ACP has subsequently been incorporated, as a business unit within Personal Products Company. Reassignment of the Patent from Advanced Care Products, Ortho Pharmaceutical Corp. to Advanced Care Products, Personal Products Co. is in process.

EXCLUSIVITY SUMMARY FOR NDA # 20-968 SUPPL 0
20-968

Trade Name Monistat® Dual-Pak™ Generic Name miconazole nitrate vaginal insert

Applicant Name Advanced Care Products HFD # 590, DSPIDP (Division of Special Pathogen and Immunologic Drug Products.

Approval Date If Known June 30, 1999.

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?

YES /✓/ NO /___/

b) Is it an effectiveness supplement? N/A.

YES /___/ NO /___/

If yes, what type? (SE1, SE2, etc.) _____

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /✓/ NO /___/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /✓/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request? 3 years.

e) Has pediatric exclusivity been granted for this Active Moiety?

No; we waived the requirement

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s)✓, dosage form×, strength×, route of administration✓, and dosing schedule×, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

note: ✓ = yes × = No.

YES /___/ NO /✓/

If yes, NDA #_____. Drug Name _____.

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /✓/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES N/A.

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including

other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

APPEARS THIS WAY
ON ORIGINAL

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /✓/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /✓/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data

would not independently support approval of the application?

YES /✓/ NO /___/

APPEARS THIS WAY
ON ORIGINAL

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /✓/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /✓/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # 96-002 P pivotal

" #2, " # 97-006 P "

" #3 " # 97-007 P (pharmacokinetic)

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /✓/

Investigation #2 YES /___/ NO /✓/

Investigation #3: None

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /✓/

Investigation #2 YES /___/ NO /✓/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #1, Study # 96-002 P

" #2, " # 96-006 P

" #3, " # 97-006 P.

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # [redacted] YES /✓/ ! NO /___/ Explain: _____

Investigation #2

IND # [redacted] YES /✓/ ! NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study? N/A

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

/S/ 8/10/1998

Signature Date

Title: Project Manager
(Regulatory Health Project Coordinator)

/S/ 6/30/1999

Signature of Office/
Division Director Date

cc: Original NDA Division File HFD-~~85~~ 93 Mary Ann Holovac

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

NDA# 20-968 (orig) Supplement # X Circle one: SE1 SE2 SE3 SE4 SE5 SE6

Trade name { Monistat® Dual-Pak TR : Monistat® Soft-Gel Vaginal Insert 1200 mg + Monistat® External Vulvar Cream

HFD-590 Trade and generic names/dosage form: miconazole nitrate Action: (AP) AE NA

Combination vaginal insert, softgel, with Miconazole external vulvar cream

Applicant Advanced Care Products (ACP) Therapeutic Class Vaginal Antifungal

Indication(s) previously approved for similar product & active ingredient: Vaginal Candidiasis

Pediatric information in labeling of approved indication(s) is adequate __ inadequate __ N/A

Proposed indication in this application Vaginal Candidiasis

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? ✓ Yes (Continue with questions) __ No (Sign and return the form)

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

__ Neonates (Birth-1month) __ Infants (1month-2yrs) __ Children (2-12yrs) ✓ Adolecents(12-16yrs)

__ 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

✓ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required. The Agency believes adult clinical trial data can be extrapolated to demonstrate safety and effectiveness in post menarchal girls, and it is unlikely that premenarchal girls would need this indication.

__ 3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

__ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

__ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

__ c. The applicant has committed to doing such studies as will be required.

- __ (1) Studies are ongoing,
- __ (2) Protocols were submitted and approved.
- __ (3) Protocols were submitted and are under review.
- __ (4) If no protocol has been submitted, attach memo describing status of discussions.

__ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

✓ 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

__ 5. If none of the above apply, attach an explanation, as necessary.

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? __ Yes ✓ No

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from Team Leader (e.g., medical review, medical officer, team leader)

/S/

Signature of Preparer and Title Project Manager June 30, 1999 Date

Orig NDA/~~BLA~~ # 20-968

HFD-590/Div File

NDA/BLA Action Package

HFD-006/ KRoberts

(revised 10/20/97)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, KHYATI ROBERTS, HFD-6 (ROBERTSK)

Advanced Care Products
Personal Products Company
691 Highway 1, P.O. Box 6024
North Brunswick, New Jersey 08902-0724

April 19, 1999

- This is exactly the same as the electronic submission of 4/27/99
- This has pediatric & geriatric

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

AMENDMENT TO PENDING APPLICATION
Pending NDA 20-968
Miconazole Nitrate Vaginal [redacted] nd External Cream

Dear Dr. Goldberger:

Reference is made to pending NDA 20-968 for the prescription use of a 1200 mg miconazole nitrate vaginal [redacted] and 2% external cream for treating vaginal candidiasis. Reference is also made to two facsimiles, dated April 6, 1999 and April 14, 1999. At this time, Advanced Care Products (ACP) is responding to the requests in both facsimiles and request that this information be made part of our pending application.

In response to the April 6, 1999 communication from FDA regarding pediatric studies, ACP would like to request a full waiver of required pediatric studies for this NDA. This drug product does not represent a meaningful therapeutic benefit over existing treatments and is not expected to be used in a substantial number of pediatric patients. It is important to note that prior to puberty, females do not get vulvovaginal candidiasis (VVC).

Also in response to the April 6 request to clarify the duration of use for the external cream, it is our intent that the external cream will be used as it is in our other combination therapies. That is, it can be applied externally twice daily for up to seven days. This was how the external cream was dosed in the studies to support the NDA. Draft labeling that reflects this -- as well as updated pediatric and geriatric use subsections (also requested April 6) is attached.

The April 14, 1999 fax from FDA (Christina Chi) requested copies of case report forms for all patients (listed below) with adverse experiences in the urinary system.

Study 96-002		**Study 97-006**	
1200 mg Group	M7C Group	1200 mg Group	M7C Group
01517	01205	03606	01303
00701	01206	01605	02603
00303	00619	02506	
01001	00703	04203	
01416	00503	00101	
01114	01311	01701	
00717		02103	
01101		04303	
01411			

Please feel free to contact me directly at 732-524-1675 if you have any questions.

Sincerely,

ADVANCED CARE PRODUCTS

Lynn J. Pawelski for

APPEARS THIS WAY
ON ORIGINAL

Diane Herron
Director, Regulatory Affairs

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)

APPEARS THIS WAY
ON ORIGINAL

Advanced Care Products
Personal Products Company
691 Highway 1
P.O. Box 6024
North Brunswick, NJ 08902-0724

January 13, 1999

Dr. Jose Carreras
Food and Drug Administration
Division of Special Investigations (HFD-344)
7520 Standish Place, Room 125
Rockville, MD 20855

RE: Pending NDA 20-968
MONISTAT® 1 DUAL PAK®
Miconazole Nitrate 1200 mg Soft Gel Insert and 2% Cream
Investigator Information

Dear Dr. Carreras:

Reference is made to pending NDA 20-968 for Miconazole Nitrate 1200 mg Vaginal [redacted] and to your December 2, 1998 request for investigator information. Advanced Care Products (ACP) is providing the investigator information requested to assist your office with the inspections of the investigators listed below. The site specific information provided herein includes a copy of the pertinent study protocol, data listings for primary endpoints, a listing of adverse events (by subject), and a listing of discontinued subjects and the reason for discontinuation. The sites/investigators are as follows:

Study 96-002

Dr. W. Ryckman Caplan
2744 Lexington Avenue
Kenner, LA 70062

Dr. Kevin Patrick ✓
San Diego State University
Student Health Services
5500 Campanile Drive
San Diego, CA 92182-4701

Study 97-006

Dr. Diana Koster ✓
Lovelace Scientific Resources, Inc.
2441 Ridgequest SE Drive
Albequerque, NM 87108

Dr. Larry Guilderman
University Clinical Research Associates, Inc.
1150 North University Drive
Pembroke Pines, FL 33024

We trust that this information fulfills your request. If there is anything else we can provide or if you have any questions, please contact me at (732) 524-1675.

Sincerely,
ADVANCED CARE PRODUCTS

APPEARS THIS WAY
ON ORIGINAL

Lynn A. Pawelski for
Diane Herron
Director, Regulatory Affairs

cc: Christina Chi, Project Manager
Division of Special Pathogens and Immunologic Drug Products

APPEARS THIS WAY
ON ORIGINAL

ORIGINAL [redacted] DRUG APPLICATION
NDA 20-968
MICONAZOLE NITRATE (1200 mg) VAGINAL [redacted]
ITEM 8: CLINICAL DATA

LIST OF INVESTIGATORS - ALPHABETICALLY

Investigator Sub-Investigator(s)	Patient No.	Study Identifier Protocol No.	Date Filed to IND No. 37,522	Study Start Date	Location in NDA		
					Full Report	Tabulations	Discontinued CRF's
Donald E. Moore, M.D. Charlie M. Browne, M.D. Catherine R. Friedman Victor Y. Fujimoto, M.D. Patricia Hardman, A.R.N.P. Paul Miller, M.D. Kirkwood K. Shy, M.D. Louis A. Vontver, M.D. Loret Waldal Fertility and Endocrine Center University of Washington 4225 Roosevelt Way NE, Suite 101 Seattle, WA 98105	01801 – 01806 03501 – 03506 05001 – 05006 05701 – 05702	97-006-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT ®-7 Vaginal Cream	6/12/97	5/27/97	Item 8 Vol. 1.9 pp. 08-000276	Item 11 Vol. 1.20 pp. 11-002426	None Submitted
John Ondrejicka, M.D. Health Trials 3000 2380 Soth Third Street Jacksonville Beach, FL 32250	Did not enroll any paticnts.	97-006-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT ®-7 Vaginal Cream	5/16/97	05/15/97	Item 8 Vol. 1.9 pp. 08-000276	Item 11 Vol. 1.20 pp. 11-002426	None Submitted
Kevin Patrick, M.D., M.S. Cheryl Pickern, RNP San Diego State University Student Health Services 5300 Campanile Drive San Diego, CA 92182-4701	00801 – 00818 01409 – 01414 01613	96-002-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT ®-7 Vaginal Cream	11/14/96	11/05/96	Item 8 Vol. 1.9 pp. 08-000171	Item 11 Vol. 1.17 pp. 11-001027	None Submitted

ORIGINAL NEW DRUG APPLICATION
NDA 20-968
MICONAZOLE NITRATE (1200 mg) VAGINAL [redacted]
ITEM 8: CLINICAL DATA
LIST OF INVESTIGATORS - ALPHABETICALLY

Investigator Sub-Investigator(s)	Patient No.	Study Identifier Protocol No.	Date Filed to IND No. 37,522	Study Start Date	Location in NDA		
					Full Report	Tabulations	Discontinued CRF's
Dan Craig Henry, M.D. Bruce Callister, PAC Peter Chapa, PAC Shane Christensen, M.D. Susan Edwards, M.D. Deb Gobelman, PAC Elizabeth Joy, M.D. Jamie Longe, M.D. Donna Mason, FNP Allen Naylor, M.D. Jack Taylor, M.D. Elizabeth Winfield, PAC Stephen Wood, M.D. Foothill Family Clinic 2295 Foothill Drive Salt Lake City, UT 84109	00401 – 00406 00601 – 00618	96-002-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT®-7 Vaginal Cream	9/19/96	09/19/96	Item 8 Vol. 1.9 pp. 08-000171	Item 11 Vol. 1.17 pp. 11-001027	None Submitted
Diana Willis Koster, M.D. Harriette Barber, CNP, MPH Martin J. Conway, M.D. Frank Snyder, M.D. Lovelace Scientific Resources 2441 Ridgecrest Drive, S.E. Albuquerque, NM 87108	01101 – 01106 02001 – 02006 02601 – 02606 03601 – 03606 04201 – 04203	97-006-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT®-7 Vaginal Cream	06/12/97	05/27/97	Item 8 Vol. 1.9 pp. 08-000276	Item 11 Vol. 1.20 pp. 11-002426	None Submitted

220000-80

ORIGINAL NEW DRUG APPLICATION
NDA 20-968
MICONAZOLE NITRATE (1200 mg) VAGINAL [redacted]
ITEM 8: CLINICAL DATA

LIST OF INVESTIGATORS - ALPHABETICALLY

Investigator Sub-Investigator(s)	Patient No.	Study Identifier Protocol No.	Date Filed to IND No. 37,522	Study Start Date	Location in NDA		
					Full Report	Tabulations	Discontinued CRF's
W. Ryckman Caplan Andrea Favalora, B.S. 4740 S. I-10 Service Road Metairie, LA 70001	00413 – 00418 00719 – 00720 00819 – 00820 01501 – 01520	96-002-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT®-7 Vaginal Cream	10/15/96	01/10/96	Item 8 Vol. 1.9 pp. 08-000171	Item 11 Vol. 1.17 pp. 11-001027	Item 12 Vol. 1.29 pp. 12-000060
Dan L. Chichester, M.D. Tina Hedin Goldsmith, R.N., M.S. Jacolin Shifrar, RN, NP 1160 East 3900 South, Suite 1050 Salt Lake City, UT 84124	00301 – 00313 00318	96-002-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT®-7 Vaginal Cream	8/28/96	09/18/96	Item 8 Vol. 1.9 pp. 08-000171	Item 11 Vol. 1.17 pp. 11-001027	Item 12 Vol. 1.29 pp. 12-000025
Larry I. Gilderman, M.D. Aleyda Borge, M.D. Gerald Hoffman, D.O. University Clinical Research Assoc. Inc. 1150 N. University Drive Pembroke Pines, FL 33024	00601 – 00606 01401 – 01406 01501 – 01506 03701 – 03706 04601 – 04606	97-006-P Phase III, Miconazole Nitrate 1200 mg Vaginal [redacted] vs. MONISTAT®-7 Vaginal Cream	5/16/97	05/14/97	Item 8 Vol. 1.9 pp. 08-000276	Item 11 Vol. 1.20 pp. 11-002426	None Submitted

AUG 8 1999

CDER LABELING AND NOMENCLATURE COMMITTEE

CONSULT #	1187	HFD# 590	PROPOSED PROPRIETARY NAME:	PROPOSED ESTABLISHED NAME:
ATTENTION:	Christina Chi		Monistat Dual-Pak	miconazole nitrate 1200 mg vaginal and 2% external cream
RE:	NDA/IND #	20-968		

A. Look-alike/Sound-alike

	Potential for confusion:
	____ Low ____ Medium ____ High
	____ Low ____ Medium ____ High
	____ Low ____ Medium ____ High
	____ Low ____ Medium ____ High
	____ Low ____ Medium ____ High

B. Misleading Aspects:

C. Other Concerns:

The sponsor should flag the label with information that the current product contains a new tablet, strength and shape of tablet.

Major reference texts (American Drug Index, Goodman and Gilmans, etc.) should be contacted by sponsor so that their information entries can be updated with new product characteristics.

D. Established Name

____ Satisfactory

____ Unsatisfactory/Reason

Recommended Established Name

E. Proprietary Name Recommendations:

XXX ACCEPTABLE ____ UNACCEPTABLE

F. Signature of Chair/Date D Boring 8/9/99

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

DATE: 4/28/99
FROM: Dan Boring, R.Ph., Ph.D., Chair, CDER Labeling and Nomenclature Committee
TO: Brad Leissa, M.D., Medical Officer, HFD-590, DSPIDP
SUBJECT: Monistat trademark applied to products containing different active ingredients

The CDER Labeling and Nomenclature Committee believes that application of the same proprietary designation to drug products that contain different active ingredients violates the principles of both 21CFR201.6(a) and 21CFR201.10 (c) (5).

21CFR201.6(a) provides that false or misleading labeling on a drug with respect to another drug, device, food or cosmetic may render the drug misbranded. The Committee believes that having two different products with the same brand name in the marketplace is inherently misleading and provides the consumer with an opportunity to inadvertently obtain an inappropriate product.

Additionally, 21CFR201.10 (c) (5), states that labeling may be misleading when designation of a drug or ingredient by a proprietary name, may be confused with the proprietary name or the established name of a different drug or ingredient, because of similarities in spelling or pronunciation. Clearly, in the case of the Monistat products, the different products can be easily confused because they have the same brand name.

It is the primary recommendation of the Committee that BMP resume use of the proprietary name VAGISTAT-1 for their otc products containing tioconazole and that MONISTAT be used for products containing miconazole. However, it is also recognized that the separate trademark MONISTAT 1 (distinct from MONISTAT) has established brand identity for products containing tioconazole. If MONISTAT 1 is retained for tioconazole products, then MONISTAT 1 Dual-Pak is inaccurate and misleading and should be changed to avoid confusion with MONISTAT 1.

Sincerely,

/S/

Dan Boring, R.Ph., Ph.D.
Chair, CDER Labeling and Nomenclature Committee

Cc: Christina Chi

faxed to me on 6/15/1999 2:36PM

DUPLICATE

Advanced Care Products
Personal Products Company
691 Highway 1, P.O. Box 6024
North Brunswick, New Jersey 08902-0724

ORIG AMENDMENT

June 15, 1999

BM

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

AMENDMENT TO PENDING APPLICATION
SAFETY UPDATE REPORT
Pending NDA 20-968
Miconazole Nitrate Vaginal [redacted] and External Cream

Dear Dr. Goldberger:

Reference is made to pending NDA 20-968 for the prescription use of a 1200 mg miconazole nitrate vaginal [redacted] and 2% external cream for treating vaginal candidiasis. Pursuant to section 505(i) of the act, Advanced Care Products (ACP) is hereby updating our pending application with safety information.

At this time, there is no new safety information to report. The original clinical database was locked prior to NDA submission (June 30, 1998). Advanced Care Products has begun enrolling patients in a large-scale safety study (enrollment began in May 1999), but safety data is not yet available. No other new studies have been conducted since the original NDA submission.

Should any additional safety data become available, we will update this NDA. Please feel free to contact me directly at 732-524-1675 if you have any questions.

Sincerely,

Lynn A. Pawelski for

Diane Herron
Director, Regulatory Affairs

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)

Advanced Care Products
Personal Products Company
691 Highway 1, P.O. Box 6024
North Brunswick, New Jersey 08902-0724

June 11, 1999

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

AMENDMENT TO PENDING APPLICATION
Pending NDA 20-968
Miconazole Nitrate Vaginal [redacted] and External Cream

Dear Dr. Goldberger:

Reference is made to pending NDA 20-968 for the prescription use of a 1200 mg miconazole nitrate vaginal [redacted] and 2% external cream for treating vaginal candidiasis. Reference is also made to a fax received today, June 11, 9999. At this time, Advanced Care Products (ACP) is responding to this fax and ask that this information be made part of our pending application.

There were two questions posed regarding stability testing on an annual batches and long term stability data. The attachment lists both the questions verbatim from the FDA fax along with ACP's response.

Per your request of June 9, 1999, our supplier has informed us that [redacted] The supplier has confirmed that they will update their DMF to include this information.

We feel that this information contained in this submission will satisfy the questions/concerns raised by FDA. Please feel free to contact me directly at 732-524-1675 if you have any questions.

Sincerely,
ADVANCED CARE PRODUCTS

Lynn A. Pawelski for

Diane Herron
Director, Regulatory Affairs

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)

Advanced Care Products
Personal Products Company
691 Highway 1, P.O. Box 6024
North Brunswick, New Jersey 08902-0724

June 7, 1999

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products, HFD-590
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

AMENDMENT TO PENDING NDA 20-968
Miconazole Nitrate 1200 mg Vaginal [redacted] and 2% External Cream

Dear Dr. Goldberger:

Reference is made to pending NDA 20-968 for the prescription use of a 1200 mg miconazole nitrate vaginal [redacted] and 2% external cream for treating vaginal candidiasis. Reference is also made to a fax dated June 4, 1999 from FDA regarding comments on labeling from the Biopharm reviewer. Listed is the comment/question from the fax, with our response directly below. The comment/question has been retyped verbatim directly from FDA's fax. Please see Attachment #1.

In addition, ACP is providing the illustrations that will be used in the Patient Package Insert in the "DIRECTIONS FOR USE" section. There are two pages containing four illustrations. The number on the illustration corresponds to the number in the instructions. Please see Attachment #2.

The updated Physician Package Insert and Patient Package Insert can be located in Attachment #3, along with an electronic copy of that labeling.

We trust that this is a complete response to the questions/comments raised. If you have any questions, please feel free to contact me at (732) 524-1675.

Sincerely,

Diane Herron,
Director, Regulatory Affairs

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)

Advanced Care Products
Personal Products Company
691 Highway 1
P.O. Box 6024
North Brunswick, NJ 08902-0724

N.C.

Received
June 3, '99

June 2, 1999

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products, HFD-590
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

AMENDMENT TO PENDING NDA 20-968
Miconazole Nitrate 1200 mg Vaginal [redacted] and 2% External Cream

Dear Dr. Goldberger:

Reference is made to pending NDA 20-968 for the prescription use of a 1200 mg miconazole nitrate vaginal [redacted] and 2% external cream for treating vaginal candidiasis. Reference is also made to our May 7, 1999 submission of a new proposed name for the subject pending NDA, MONISTAT® DUAL-PAK. As per an agency request for additional information made on May 25, 1999, Advanced Care Products (ACP) is providing information related to the status of a previous "Dual-Pak" product we marketed.

[redacted] MONISTAT® DUAL-PAK (miconazole nitrate 200 mg vaginal suppositories with miconazole nitrate 2% cream), until June 1996. The last batch of product was manufactured in March 1996 and carried a 3 year expiration date, which results in the last batch shipped having an expiration date of March 1999. We therefore confirm that none of this product remains on the market at this time.

In addition, ACP commits that we will notify pertinent trade publications (e.g., USP DI, Martindales, AHFS Drug Information, etc.) regarding the difference between the MONISTAT DUAL-PAK product previously [redacted] and the subject product, MONISTAT DUAL-PAK prior to launch.

We trust that this is a complete response to the issues raised. If you have any questions, please feel free to contact me at (732) 524-1675. We look forward to achieving a timely resolution to this issue.

Sincerely,

Diane Herron

Diane Herron
Director, Regulatory Affairs

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)

Advanced Care Products
691 Highway 1, P.O. Box 6024
North Brunswick, New Jersey 08902-0724

May 4, 1999

Mark Goldberger, M.D.
Director
Food and Drug Administration
Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
9201 Corporate Boulevard
Rockville, MD 20850

Amendment to Pending Application
NDA 20-968
Miconazole Nitrate 1200 mg Vaginal [redacted] and 2% External Cream

Dear Dr. Goldberger:

Reference is made to a question received from the agency on May 4, 1999 regarding the Environmental Assessment (EA) submitted as part of the subject New Drug Application (NDA). It was requested that we formally claim categorical exclusion based on the information provided in the Environmental Assessment submitted in our original NDA submitted June 30, 1998 (Vol. 1.3, p. 03-000691).

At this time, Advanced Care Products is claiming a categorical exclusion for the subject new drug application. Per §25.31(b), the subject NDA qualifies for a categorical exclusion as the action increases the use of the active moiety, but the estimated concentration at the point of entry into the aquatic environment will be [redacted] Advanced Care Products has no knowledge of extraordinary circumstances that would affect this concentration calculation.

Should you have any questions regarding this amendment or the claimed categorical exclusion, please contact me directly at (732) 524-1675.

Very truly yours,

Lynn A. Pawelski for

Diane Herron
Director, Regulatory Affairs
Advanced Care Products

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)